

NATIONAL GUIDELINE CLEARINGHOUSE™ (NGC™)  
GUIDELINE SYNTHESIS

SCREENING FOR BREAST CANCER

Guidelines

1. Royal New Zealand College of General Practitioners (RNZCGP). [Early detection of breast cancer](#). Wellington (New Zealand): Royal New Zealand College of General Practitioners; 1999. 61 p. [176 references]
2. Canadian Task Force on Preventive Health Care (CTFPHC).
  - [Preventive health care, 2001 update: screening mammography among women aged 40-49 years at average risk of breast cancer](#). CMAJ 2001 Feb 20;164(4):469-76. [76 references]
  - [Preventive health care, 2001 update: should women be routinely taught breast self-examination to screen for breast cancer?](#) CMAJ 2001 Jun 26;164(13):1837-46. [78 references]
3. Brigham and Women's Hospital (BWH). [Breast disease. Guide to prevention, diagnosis and treatment](#). Boston (MA): Brigham and Women's Hospital; 2001. 9 p. [13 references]
4. U.S. Preventive Services Task Force (USPSTF). [Screening for breast cancer: recommendations and rationale](#). Ann Intern Med 2002 Sep 3;137(5 Part 1):344-6. [10 references]
5. American Cancer Society (ACS). [ACS guidelines for breast cancer screening: update 2003](#). CA Cancer J Clin 2003 May-Jun;53(3):141-69. [184 references]

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## GUIDELINE CONTENT COMPARISON

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### INTRODUCTION:

A direct comparison of RNZCGP, CTFPHC, BWH, USPSTF, and ACS recommendations for screening asymptomatic women for breast cancer is provided in the tables below. The guidelines differ somewhat in scope. RNZCGP's guideline, for example, also includes recommendations for risk assessment, diagnostic recommendations for women with symptoms suggestive of breast cancer, and information for cultural considerations for Maori women. BWH's guideline, which is based on detailed clinical algorithms, also provides recommendations for breast cancer risk determination and for managing benign breast symptoms and other common breast problems such as mastalgia. The scope of the ACS guideline differs from the others in that it examines alternative screening modalities for women at increased risk and potential new imaging technologies for women at average risk of breast cancer. The ACS guideline also gives special focus to the screening of older women and women with comorbid conditions.

[Table 1](#) gives a broad overview of the scope of the five guidelines; [Table 2](#) details the recommendations for mammographic screening as well as for other screening strategies; [Table 3](#) specifies the potential benefits and harms associated with breast cancer screening.

The evidence supporting the major recommendations is also identified, with the definitions of the rating schemes used by RNZCGP, CTFPHC, and USPSTF included in [Table 4](#).

Following the content comparison, areas of agreement and differences among the guidelines are discussed.

Listed below are common abbreviations used within the tables and discussions:

- ACS, American Cancer Society
- BSE, breast self-examination
- BWH, Brigham and Women's Hospital
- CBE, clinical breast examination
- CTFPHC, Canadian Task Force on Preventive Health Care
- DCIS, Ductal carcinoma in situ
- RNZCGP, Royal New Zealand College of General Practitioners
- USPSTF, United States Preventive Services Task Force

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| TABLE 1: SCOPE |
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| Objective         |   |
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| RNZCGP (1999)     | <ul style="list-style-type: none"> <li>To help primary care providers provide consistent advice to women about the risk factors for and the early detection and diagnosis of breast cancer</li> <li>To provide information about cultural considerations for Maori, which may be useful for improving the service effectiveness that primary care providers can offer</li> </ul>  |
| CTFPHC (2001)     | <ul style="list-style-type: none"> <li>To make recommendations on (1) screening mammography in asymptomatic Canadian women aged 40 to 49 years at average risk of breast cancer and (2) teaching of breast self-examination in asymptomatic women of all ages in the general population</li> </ul>  |
| BWH (2001)        | <ul style="list-style-type: none"> <li>To provide physicians with clear guidelines for screening as well as clinical pathways for risk counseling, diagnosis, and treatment of symptomatic breast disease</li> <li>To distinguish the roles of the primary care physician, Breast Center, and breast surgeon</li> </ul>   |
| USPSTF (2002)     | <ul style="list-style-type: none"> <li>To update the 1996 recommendations on screening for breast cancer in women at average or high risk</li> </ul>  |
| ACS (2003)        | <ul style="list-style-type: none"> <li>To review the existing American Cancer Society (ACS) guidelines for the early detection of breast cancer based on evidence that has accumulated since the last revision in 1997</li> </ul>   |
| Target Population |   |
| RNZCGP (1999)     | <ul style="list-style-type: none"> <li>New Zealand</li> <li>Asymptomatic and symptomatic women <ul style="list-style-type: none"> <li>Women aged 50-74 years without symptoms suggestive of breast cancer</li> <li>High-risk asymptomatic women aged 40 and over</li> </ul> </li> </ul> <p>Note: Women with symptoms suggestive of breast cancer and Maori women are considered in the guideline, but these target populations are not addressed in this synthesis.</p> |
| CTFPHC (2001)     | <ul style="list-style-type: none"> <li>Canada</li> <li>Asymptomatic women aged 40 to 49 at average risk of breast cancer (mammography screening)</li> <li>Asymptomatic women of all ages in the general population</li> </ul>   |

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|                                    | (routine teaching of breast self-examination)   |
| BWH<br>(2001)                      | <ul style="list-style-type: none"> <li>• United States</li> <li>• Women 20 years of age and older (universal screening recommendation for clinical breast exam and breast self-exam)</li> <li>• Women 40 years of age and older (universal screening recommendation for mammography)</li> </ul> <p>Note: Women with palpable breast masses or mastalgia are also considered in the guideline for diagnostic and treatment recommendations, and women at high risk of breast cancer are considered for recommendations for genetic counseling or chemoprevention. These topics, however, are not considered in this synthesis.</p> |
| USPSTF<br>(2002)                   | <ul style="list-style-type: none"> <li>• United States</li> <li>• Women aged 40 years and older</li> </ul>  |
| ACS<br>(2003)                      | <ul style="list-style-type: none"> <li>• United States</li> <li>• Women aged 40 years or older</li> </ul>   |
| Intended Users                     |   |
| RNZCGP<br>(1999)                   | Advanced Practice Nurses; Nurses; Physicians  |
| CTFPHC<br>(2001)                   | Advanced Practice Nurses; Physicians; Physician Assistants; Allied Health Care Practitioners  |
| BWH<br>(2001)                      | Advanced Practice Nurses; Health Care Providers; Physician Assistants; Physicians   |
| USPSTF<br>(2002)                   | Advanced Practice Nurses; Physicians; Nurses; Physician Assistants; Allied Health Care Practitioners; Students  |
| ACS<br>(2003)                      | Advanced Practice Nurses; Allied Health Personnel; Health Care Providers; Health Plans; Hospitals; Managed Care Organizations; Nurses; Patients; Physician Assistants; Physicians; Public Health Departments  |
| Screening Interventions Considered |   |
| RNZCGP<br>(1999)                   | <ul style="list-style-type: none"> <li>• Risk assessment (identifying risk factors for developing breast cancer, such as gender, age, family history, medical history, radiation exposure; genetic testing for BRCA 1 and 2 genes)</li> <li>• Breast cancer screening</li> </ul>  |

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|               | <ul style="list-style-type: none"> <li>• Mammography alone or with clinical breast examination (CBE)</li> <li>• Breast self-examination (BSE)</li> </ul> <p>Note: Additional diagnostic procedures (the triple test: CBE, diagnostic mammography, fine needle aspiration biopsy; diagnostic ultrasound; core biopsy; and other diagnostic modalities) are considered in the guideline but are not addressed in this synthesis</p>  |
| CTFPHC (2001) | <ul style="list-style-type: none"> <li>• Mammographic breast cancer screening</li> <li>• Routine teaching of BSE as part of the periodic health examination</li> </ul> <p>Excluded Topics: CBE, mammographic screening in populations other than asymptomatic women aged 40-49 years</p>   |
| BWH (2001)    | <p>Breast cancer screening</p> <ul style="list-style-type: none"> <li>• Mammography</li> <li>• CBE</li> <li>• BSE</li> </ul> <p>Note: Assessment of risk factors for breast cancer and surveillance of major risk factors, including genetic predisposition and genetic counseling are also considered, but specific recommendations for screening of high-risk women are not given. Additional diagnostic procedures, including ultrasound, image-guided core biopsy, and image-guided aspiration, as needed, are discussed in the guideline but are not addressed in this synthesis.</p> |
| USPSTF (2002) | <p>Routine screening with mammography alone or mammography and annual CBE</p> <ul style="list-style-type: none"> <li>• CBE alone</li> <li>• BSE</li> </ul>   |
| ACS (2003)    | <ul style="list-style-type: none"> <li>• Breast cancer screening in women of average risk <ul style="list-style-type: none"> <li>• Annual mammography beginning at age 40</li> <li>• CBE</li> <li>• BSE</li> </ul> </li> <li>• Screening of older women with comorbid conditions</li> <li>• Screening of women at high risk</li> </ul> <p>Note: Additional screening modalities such as ultrasound and magnetic resonance imaging (MRI) were considered but evidence was insufficient for making a formal recommendation.</p>  |

TABLE 2: COMPARISON OF RECOMMENDATIONS FOR BREAST CANCER SCREENING

| COMPARISON OF RECOMMENDATIONS FOR MAMMOGRAPHIC SCREENING |  |
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| RNZCGP (1999)  | <p>Mammography is the principle screening procedure for breast cancer (in women with no symptoms).</p> <ul style="list-style-type: none"> <li>• For women under age 40, screening mammography is not recommended</li> <li>• For women aged 40-49, annual routine mammography is not advised unless they are higher risk (as defined in the guideline). [Level I]</li> <li>• For higher risk women (as defined in the guideline) over the age of 40, annual mammography is recommended. [Level III-2]</li> <li>• For women aged 50-74 two-yearly mammography is recommended. [Level I]</li> </ul>   |
| CTFPHC (2001)  | <ul style="list-style-type: none"> <li>• Women 40 to 49 years old: Current evidence regarding the effectiveness of screening mammography does not suggest the inclusion of the maneuver in, or its exclusion from, the periodic health examination of women aged 40 to 49 at average risk of breast cancer (grade C recommendation). Upon reaching the age of 40, Canadian women should be informed of the potential benefits and risks of screening mammography and assisted in deciding at what age they wish to initiate the maneuver.</li> <li>• Women 50 to 69 years old: The guideline update on mammography screening does not address this population group.</li> <li>• Women <math>\geq</math> 70 years old: The guideline update on mammography screening does not address this population group.</li> <li>• Women at increased risk for breast cancer: The guideline update on mammography screening does not address this population group.</li> </ul> |
| BWH (2001)   | <ul style="list-style-type: none"> <li>• Women aged 50-69 years: It is well established that annual mammography reduces breast cancer mortality by about 30% in women age 50 to 69.</li> <li>• Women aged 40-49 years: Brigham and Women's and Faulkner Hospitals support the recommendation of annual screening mammograms for women in this age group.</li> <li>• Women aged &gt;69 years: No recommendations offered.</li> </ul>  |
| USPSTF (2002)  | <p>For women aged 40 and over, the U.S. Preventive Services Task Force recommends screening mammography, with or without clinical breast examination, every 1-2 years. (B recommendation).</p> <p>Clinical Considerations</p>  |

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|            | <ul style="list-style-type: none"> <li>• The precise age at which the benefits from screening mammography justify the potential harms is a subjective judgment and should take into account patient preferences. Clinicians should inform women about the potential benefits (reduced chance of dying from breast cancer), potential harms (e.g., false-positive results, unnecessary biopsies), and limitations of the test that apply to women their age. Clinicians should tell women that the balance of benefits and potential harms of mammography improves with increasing age for women between the ages of 40 and 70.</li> <li>• Women who are at increased risk for breast cancer (e.g., those with a family history of breast cancer in a mother or sister, a previous breast biopsy revealing atypical hyperplasia, or first childbirth after age 30) are more likely to benefit from regular mammography than women at lower risk. The recommendation for women to begin routine screening in their 40s is strengthened by a family history of breast cancer having been diagnosed before menopause.</li> <li>• For women aged 50 and older, there is little evidence to suggest that annual mammography is more effective than mammography done every other year.</li> <li>• For women aged 40-49, available trials also have not reported a clear advantage of annual mammography over biennial mammography. Nevertheless, some experts recommend annual mammography based on the lower sensitivity of the test and on evidence that tumors grow more rapidly in this age group.</li> <li>• Older women (over age 69 years): The precise age at which to discontinue screening mammography is uncertain. Only two randomized controlled trials enrolled women older than 69, and no trials enrolled women older than 74. Older women face a higher probability of developing and dying from breast cancer but also have a greater chance of dying from other causes. Women with comorbid conditions that limit their life expectancy are unlikely to benefit from screening.</li> </ul> |
| ACS (2003) | <ul style="list-style-type: none"> <li>• Women age 40-69 years: Women at average risk should begin annual mammography at age 40. Women should have an opportunity to become informed about the benefits, limitations, and potential harms associated with regular screening.</li> <li>• Older women (over age 69): Screening decisions in older women should be individualized by considering the potential benefits and risks of mammography in the context of current health status and estimated life expectancy. As long as a woman is in reasonably good health and would be a candidate for treatment, she should continue to be screened with mammography.</li> <li>• High-risk women: Women at increased risk of breast cancer might benefit from additional screening strategies beyond those offered to women of average risk, such as earlier initiation of screening, shorter screening intervals, or the addition of</li> </ul>   |

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|  | <p>screening modalities other than mammography and physical examination, such as ultrasound or magnetic resonance imaging. However, the evidence currently available is insufficient to justify recommendations for any of these screening approaches.</p>  |
| <p>COMPARISON OF RECOMMENDATIONS REGARDING CLINICAL BREAST EXAMINATION AND BREAST SELF-EXAMINATION</p> |   |
| <p>RNZCGP (1999)</p>   | <ul style="list-style-type: none"> <li>• CBE may be used in conjunction with mammography screening. [Level I] Mammography is more sensitive than CBE in screening asymptomatic women, but the sensitivity of both CBE and mammography combined is greater than either alone.</li> <li>• While there have been many studies to date, methodological problems in many and the variable findings make it unclear as to any benefit that might accrue from BSE in asymptomatic women. As a result, it is suggested that (1) women, especially those over 40, should be advised to regularly look and feel for breast changes, rather than follow a systematic method of examination; (2) primary care providers should advise women that changes could indicate cancer is present and to report any changes promptly to their doctor; (3) all women who have symptoms suggestive of breast cancer should be encouraged to consult their doctor regardless of the results of recent mammograms.</li> </ul>   |
| <p>CTFPHC (2001)</p>   | <ul style="list-style-type: none"> <li>• Women aged 50 to 69: Because there is fair evidence of no benefit, and good evidence of harm, there is fair evidence to support the recommendation that routine teaching of BSE be excluded from the periodic health examination [grade D recommendation, Level I, II-1, II-3 evidence].</li> <li>• Women aged 40 to 49: Because there is fair evidence of no benefit, and good evidence of harm, there is fair evidence to support the recommendation that routine teaching of BSE be excluded from the periodic health examination [grade D recommendation, level I, II-1, II-3 evidence].</li> </ul> <p>While the evidence indicates no benefit from routine instruction, some women will request teaching in BSE. The pros and cons should be discussed with the woman, and if breast self-examination is taught, care must be taken to ensure that breast self-examination is conducted in a proficient manner.</p> <p>Note: There is insufficient evidence for effectiveness of routine teaching of BSE in women younger than 40 or older than 70 years, thus precluding making recommendations for teaching breast self-examination to women in these age groups.</p> |
| <p>BWH (2001)</p>  | <ul style="list-style-type: none"> <li>• A CBE should be performed annually in all women 20 and older. It should include inspection of the nipple for recent inversion or</li> </ul>  |



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|               | <p>excoriation and examination of the skin for erythema and retraction. To check for retraction, the patient is asked to place her hands on her waist and contract her pectoralis muscles, then to bring her arms over her head. Palpation should begin with the periclavicular and axillary nodes and should progress to a systematic examination of the entire breast, including tissue overlying the sternum, the inframammary fold and the retroareolar area.</p> <ul style="list-style-type: none"> <li>• Optimally, BSE is performed 5 to 7 days after the onset of menstruation, when the breast tissue is least engorged in premenopausal women and on the same day of the month for postmenopausal women. Randomized controlled clinical trials have shown no reduction in mortality from breast cancer among women who performed monthly BSE. However, since BSE is inexpensive and noninvasive, most physicians recommend it as a screening method to their patients. Patients who find BSE to be anxiety-provoking can be reassured that annual clinical breast examination and screening mammography are sufficient for breast cancer screening.</li> </ul> |
| USPSTF (2002) | <ul style="list-style-type: none"> <li>• The evidence is insufficient to recommend for or against routine CBE alone to screen for breast cancer. (I recommendation)</li> <li>• The evidence is insufficient to recommend for or against teaching or performing routine BSE. (I recommendation.)</li> <li>• Clinicians who advise women to perform BSE or who perform routine CBE to screen for breast cancer should understand that there is currently insufficient evidence to determine whether these practices affect breast cancer mortality, and that they are likely to increase the incidence of clinical assessments and biopsies.</li> </ul>  |
| ACS (2003)    | <ul style="list-style-type: none"> <li>• For average-risk asymptomatic women in their 20's and 30's, it is recommended that CBE be part of a periodic health examination, preferably at least every three years. Asymptomatic women aged 40 and over should continue to receive a clinical breast examination as part of a periodic health examination, preferably annually.</li> <li>• Beginning in their 20's, women should be told about the benefits and limitations of BSE. The importance of prompt reporting of any new breast symptoms to a health professional should be emphasized. Women who choose to do BSE should receive instruction and have their technique reviewed on the occasion of a periodic health examination. It is acceptable for women to choose not to do BSE or to do BSE irregularly.</li> </ul>  |

TABLE 3. BENEFITS/HARMS OF BREAST CANCER SCREENING

| POTENTIAL BENEFITS ASSOCIATED WITH BREAST CANCER SCREENING |  |
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| RNZCGP<br>(1999)   | <ul style="list-style-type: none"> <li>Breast screening reduces breast cancer mortality by 20% to 38% in women aged between 50 and 64 years. It has been estimated 480 lives could be saved over the first five years if mammography screening is provided to the entire female population aged 50-69.</li> <li>Screening mammography has a high sensitivity (80-95%) and specificity (93-95%) and both of these measures generally increase with a patient's age. Regular two-yearly screening mammography results in a reduction of breast cancer mortality by approximately 30% for women aged 40-74. Specifically, mortality is reduced 26-34% in women aged over 65 and 20-38% in women aged 50-64 by two-yearly mammography screening.</li> </ul>  |
| CTFPHC<br>(2001)   | <p>Potential reduction in mortality rates: Relative risk reduction of 18% to 45% for breast cancer mortality at 10 years was shown in two trials and one meta-analysis; no benefit was shown in six other trials. (The only trial that enrolled Canadian women failed to show an effect of screening mammography, possibly because of low power.)</p> <p>Other Positive Effects of Screening Mammography in Women Ages 40 to 49</p> <ul style="list-style-type: none"> <li>Detection of tumour at earlier stage (possibly predictive of less toxic treatment)</li> <li>Improved cosmesis</li> <li>Reassurance (72% of cases)</li> <li>Reduced anxiety about cancer at time of screening</li> </ul>   |
| BWH<br>(2001)  | <ul style="list-style-type: none"> <li>There is increasing evidence that mammographic screening alone can reduce the breast-cancer death rate by 30%, primarily through the identification of smaller, node negative invasive breast cancers. Studies have shown that compliance with screening is significantly increased by in-person and telephone counseling, especially in minority populations. Advances in biopsy techniques, surgery, chemotherapy, hormonal treatment, and supportive therapy have substantially reduced morbidity. The identification of high-risk women and the use of tamoxifen for chemoprevention and prophylaxis have demonstrated potential in preventing the disease in the most vulnerable population.</li> <li>The primary care physician can play an important role in further reducing the morbidity and mortality associated with the disease by encouraging women to undergo screening and by referring women who have findings suggestive of breast cancer to the</li> </ul> |

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|   | appropriate channels for diagnosis and treatment.   |
| USPSTF (2002)   | <ul style="list-style-type: none"> <li>• The USPSTF found fair evidence that mammography screening every 12-33 months significantly reduces mortality from breast cancer. Evidence is strongest for women aged 50-69, the age group generally included in screening trials. For women aged 40-49, the evidence that screening mammography reduces mortality from breast cancer is weaker, and the absolute benefit of mammography is smaller, than it is for older women. Most, but not all, studies indicate a mortality benefit for women undergoing mammography at ages 40-49, but the delay in observed benefit in women younger than 50 makes it difficult to determine the incremental benefit of beginning screening at age 40 rather than at age 50. The absolute benefit is smaller because the incidence of breast cancer is lower among women in their 40s than it is among older women.</li> <li>• The USPSTF concluded that the evidence is also generalizable to women aged 70 and older (who face a higher absolute risk of breast cancer) if their life expectancy is not compromised by comorbid disease. The absolute probability of benefits of regular mammography increases along a continuum with age, whereas the likelihood of harms from screening (false-positive results and unnecessary anxiety, biopsies, and cost) diminishes from ages 40-70.</li> <li>• The balance of benefits and potential harms, therefore, grows more favorable as women age. The precise age at which the potential benefits of mammography justify the possible harms is a subjective choice.</li> </ul> |
| ACS (2003)  | <ul style="list-style-type: none"> <li>• Decreased breast cancer morbidity and mortality due to early detection.</li> <li>• A meta-analysis of seven randomized controlled trials (RCTs) showed a 24% mortality reduction associated with an invitation to screening.</li> <li>• Evidence from service screening (i.e., screening in the community setting) demonstrates that modern, organized screening programs with high rates of attendance can achieve breast cancer mortality reductions equal to or greater than those observed in RCTs. Evaluation of service screening is an important new development because it measures the value of modern mammography in the community and it measures the benefit of mammography screening to women who actually get screened.</li> </ul>   |
| POTENTIAL HARMS ASSOCIATED WITH BREAST CANCER SCREENING |   |
| RNZCGP (1999)   | False positives. These can lead to unnecessary investigations ranging from repeat mammography to ultrasound, fine needle  |

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|               | <p>aspiration biopsy and/or biopsy. There is a significant false positive rate for mammography screening (0.9-6.5%), which substantially contributes to the costs associated with screening. In New Zealand, the risk of a false positive for a woman at some point during a 20-year screening programme (aged 50-69) has been calculated at 34%.</p> <p>False negatives. As with any investigation a negative result may occur even though cancer is present. The sensitivity of screening mammography is 86-94% depending on age. Thus the false negative rate is 6-14%.</p> <p>Over-treatment. There is a potential for a screening programme to detect a cancer in a woman who might never have presented clinically before dying from another cause. Thus screening may increase morbidity while not reducing mortality.</p>  |
| CTFPHC (2001) | <p>Negative Effects of Screening Mammography</p> <ul style="list-style-type: none"> <li>• Radiation-induced carcinoma</li> <li>• Unnecessary biopsies (0.6% to 0.9% of cases in Sweden, 5% to 9% of cases in U.S.)</li> <li>• Psychological stress of call-back (40% of cases)</li> <li>• Additional x-ray films (3% to 13% of cases in Sweden, 56% of cases in U.S.)</li> <li>• Possible false reassurance or false positive results</li> </ul>   |
| BWH (2001)    | <p>False positives. Data indicates that over a 10-year period, the cumulative risk of a false positive mammogram is about 50%, and the rate of benign biopsy approaches 20%.</p>   |
| USPSTF (2002) | <p>False positives. Similar to other cancer screening tests, the large majority (80% to 90%) of abnormal screening mammograms or CBEs are false-positives. These may require follow-up testing or invasive procedures such as breast biopsy to resolve the diagnosis, and can result in anxiety, inconvenience, discomfort, and additional medical expenses. The consequences of false-positive mammograms are uncertain. Most, but not all, studies report increased anxiety from an abnormal mammogram. At the same time, some studies report that women in the United States may be willing to accept a relatively high number of false-positive results in the population in return for the benefits of mammography. Studies do not indicate that false-positive results diminish adherence to subsequent screening.</p> <p>False negatives. False-negatives also occur with mammograms and CBE. Although false-negative results might provide false reassurance, the USPSTF found no data indicating these led to further delays in diagnosis.</p> <p>Over-diagnosis and treatment. Some experts view the over-</p> |

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|                       | <p>diagnosis and treatment of ductal carcinoma in situ (DCIS) as a potential adverse consequence of mammography. Although the natural history of DCIS is variable, many women in the United States are treated aggressively with mastectomy or lumpectomy and radiation. Given the dramatic increase in the incidence of DCIS in the past two decades (750%) and autopsy series suggesting that there is a significant pool of DCIS among women who die of other causes, screening may be increasing the number of women undergoing treatment for lesions that might not pose a threat to their health.</p> <p>Radiation risks. A final potential concern about mammography is radiation-induced breast cancer, but there are few data to directly assess this risk. A 1997 review, using risk estimates provided by the Biological Effects of Ionizing Radiation report of the National Academy of Sciences, estimated that annual mammography of 100,000 women for 10 consecutive years beginning at age 40 would result in up to 8 radiation-induced breast cancer deaths.</p>   |
| <p>ACS<br/>(2003)</p> | <p>Limitations and harms of breast cancer screening include false negatives, false positives, over-treatment, and radiation.</p> <p>False Negatives/False Positives</p> <p>False negatives can be attributed to inherent technological limitations of mammography, quality assurance failures, and human error; false positives also can be attributed to these factors as well as to heightened medical-legal concerns over the consequence of missed cancers. Further, in some instances, a patient's desire for definitive findings in the presence of a low-suspicion lesion also contributes to false positives. The consequences of these errors include missed cancers, with potentially worse prognosis, as well as anxiety and harms associated with interventions for benign or nonobligate precursor lesions.</p> <p>The evidence suggests that some women experience anxiety related to screening and a greater percentage experience anxiety related to false-positive results, but for most women psychological distress is short-lived and does not have lasting consequences on either stress levels or likelihood of subsequent screening.</p> <p>Overtreatment</p> <p>Since some ductal carcinoma in situ (DCIS) is not progressive, diagnostic evaluation and treatment of DCIS lesions that would not progress to invasive disease is a harm associated with screening, although the extent of harm is uncertain, as is how it might be avoided. Overtreatment of a progressive DCIS lesion that could be cured with less aggressive treatment also represents a harm, although it should not be attributed to screening.</p> |

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|  | <p><b>Radiation</b></p> <p>Several studies have provided evidence for an increased risk of breast cancer after therapeutic radiation exposure or multiple exposures to diagnostic radiation. Overall risk from single and cumulative diagnostic exposures is small, but risk increases with the amount of exposure and with younger age at exposure. Thus, it is theoretically possible that cumulative radiation exposure associated with screening mammography increases the risk of breast cancer. It has also been hypothesized that some women at increased inherited risk for breast cancer may also have increased radiation sensitivity, which could increase their risk for radiation-induced breast cancer.</p> <p>Women whose regular screening begins at an early age (e.g., age 30) may have a higher potential for radiation-induced cancers.</p> |
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TABLE 4. EVIDENCE AND RECOMMENDATION RATING SCHEMES

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| RNZCGP<br>(1999) | <p>Levels of Evidence:</p> <p>I Evidence obtained from systematic review of all relevant randomised controlled trials (RCTs).</p> <p>II Evidence obtained from at least one properly designed RCT.</p> <p>III -1 Evidence obtained from well designed controlled trials without randomisation.</p> <p>III -2 Evidence obtained from well designed cohort or case controlled analytic studies, preferably from more than one centre or research group.</p> <p>III -3 Evidence obtained from multiple time-series with or without the intervention. Dramatic results in uncontrolled experiments such as the introduction of penicillin treatment in the 1940s could be regarded as this type of evidence.</p> <p>IV-1 Evidence from descriptive studies including case series, case reports and cross-sectional studies.</p> <p>IV-2 Published policies, recommendations or opinions of recognised experts, organisations, or learned colleagues. Including endorsement of Level IV-3 evidence by recognised bodies.</p> <p>IV-3 Consensus opinion of the working party not endorsed formally</p> |
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|               | <p>by recognised bodies.</p> <p>N/A Not applicable - not possible to apply a level of evidence.</p>   |
| CTFPHC (2001) | <p>Levels of evidence:</p> <p>I - Evidence from at least one properly randomized controlled trial (RCT).</p> <p>II-1 - Evidence from well-designed controlled trials without randomization.</p> <p>II-2 - Evidence from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group.</p> <p>II-3 - Evidence from comparisons between times or places with or without the intervention. Dramatic results from uncontrolled experiments could also be included here.</p> <p>III - Opinions of respected authorities, based on clinical experience, descriptive studies or reports of expert committees.</p> <p>Grades of recommendations:</p> <p>A - Good evidence to support the recommendation that the condition or maneuver be specifically considered in a periodic health examination (PHE)</p> <p>B - Fair evidence to support the recommendation that the condition or maneuver be specifically considered in a periodic health examination</p> <p>C - Poor evidence regarding inclusion or exclusion of the condition or maneuver in a periodic health examination, but recommendations may be made on other grounds</p> <p>D - Fair evidence to support the recommendation that the condition or maneuver be specifically excluded from consideration in a periodic health examination</p> <p>E - Good evidence to support the recommendation that the condition or maneuver be specifically excluded from consideration in a periodic health examination</p> |
| USPSTF (2002) | <p>USPSTF grades the quality of the overall evidence for a service on a three-point scale (good, fair, or poor).</p> <p>Good<br/>Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess</p>   |

effects on health outcomes.

#### Fair

Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies; generalizability to routine practice; or indirect nature of evidence on health outcomes.

#### Poor

Evidence is insufficient to assess the effects on health outcomes because of limited number of power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

The USPSTF grades its recommendations according to one of five classifications (A, B, C, D, or I), reflecting the strength of evidence and magnitude of net benefit (benefits minus harms).

#### A

The USPSTF strongly recommends that clinicians routinely provide [the service] to eligible patients. (The USPSTF found good evidence that [the service] improves important health outcomes and concludes that benefits substantially outweigh harms.)

#### B

The USPSTF recommends that clinicians routinely provide [the service] to eligible patients. (The USPSTF found at least fair evidence that [the service] improves health outcomes and concludes that benefits outweigh harms.)

#### C

The USPSTF makes no recommendation for or against routine provision of [the service]. (The USPSTF found at least fair evidence that [the service] can improve health outcomes but concludes that the balance of benefits and harms is too close to justify a general recommendation.)

#### D

The USPSTF recommends against routinely providing [the service] to asymptomatic patients. (The USPSTF found at least fair evidence that [the service] is ineffective or that harms outweigh benefits.)

#### I

The USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing [the service]. (Evidence that [the service] is effective is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.)



## GUIDELINE CONTENT COMPARISON

The Royal New Zealand College of General Practitioners (RNZCGP), the Canadian Task Force on Preventive Health Care (CTFPHC), Brigham and Women's Hospital (BWH), the U.S. Preventive Services Task Force (USPSTF), and the American Cancer Society (ACS) present recommendations for screening mammography for breast cancer based on evidence available at the time of each report and provide explicit reasoning behind their judgments. CTFPHC's guideline update on screening mammography limits its recommendations to women aged 40-49 years at average risk of breast cancer. The guidelines also evaluate other screening interventions for breast cancer, such as teaching breast self-examination in the periodic health examination and clinical breast examination. The RNZCGP guideline also provides recommendations for assessing risk factors for breast cancer and for diagnostic investigations in symptomatic women. In addition, RNZCGP provides recommendations for clinical considerations for the Maori population of New Zealand. The guideline from BWH differs from the others in that it includes recommendations and an algorithm for managing benign breast symptoms such as mastalgia. The BWH algorithm also attempts to delineate the various roles of the primary care provider, the Breast Center, and the breast surgeon in the care of the woman with breast disease. The ACS guideline, while primarily focused on breast cancer screening using traditional methods, also examines new screening technologies as well as issues pertinent to screening older women and high-risk women.

### Areas of Agreement

#### Mammographic Screening for Women Aged 50-69 Years

BWH, RNZCGP, USPSTF, and ACS agree that routine screening mammography is indicated in women aged 50 to 69. Both BWH and ACS endorse annual screening, while USPSTF recommends either annual or biennial screening, and RNZCGP recommends biennial screening. CTFPHC does not offer recommendations for this age group in its 2001 guideline update.

#### Screening of Women with Selected Risk Factors for Breast Cancer

There is general agreement between RNZCGP and USPSTF concerning the value of annual screening in high-risk women. RNZCGP recommends that women over age 40 at high risk for breast cancer should receive annual mammographic screening. USPSTF states that the recommendation for women to begin routine screening in their 40s is "strengthened by a family history of breast cancer having been diagnosed before menopause."

While ACS recommends annual screening of all women beginning at age 40, it also states that high-risk women might benefit from additional screening strategies. These strategies could include initiation of screening at age 30 years or younger, shorter mammographic screening intervals (e.g., every six months), and the addition of magnetic resonance imaging or ultrasound screening. ACS cautions, however, that there is insufficient evidence to justify recommending these options in high-risk women, and it emphasizes the need for further clinical data on screening women at increased risk.

## Mammographic Screening of Older Women ( $\geq 70$ years)

The three organizations (RNZCGP, ACS, and USPSTF) that address this older population group generally agree that there is no clear age at which mammographic screening should be discontinued. Rather, the decision to screen should be made on an individual basis, taking into account personal preferences and weighing individual risks and benefits.

## Areas of Differences

### Mammographic Screening of Women Aged 40-49 Years at Average Risk of Breast Cancer

The value of routine screening of women aged 40-49 years at average risk of breast cancer is an area of controversy among the guideline groups. Much of the controversy is due to the quality and interpretation of clinical trial data regarding mortality benefits of mammographic screening.

ACS and BWH recommend routine annual mammographic screening, and USPSTF recommends annual or biennial screening in this age group. The groups acknowledge that the evidence for absolute benefit from screening of women younger than 50 years is weaker than the evidence for older women; however, a mortality benefit for women aged 40-49 has still been shown in some clinical trials. USPSTF's most recent (2002) recommendation concerning routine mammographic screening for women younger than age 50 is a change from its 1996 guideline, which found insufficient evidence to recommend for or against screening in this age group. The USPSTF has reviewed seven RCTs enrolling women aged 40-49, six of which were at least of "fair" quality. One of the trials was designed to specifically address benefits of screening in this age group and reported no reduction in breast cancer mortality with annual mammography and clinical breast examination. Of the remaining five trials, one reported significant mortality reductions, three non-significant mortality reductions, and one found no benefit. A meta-analysis pooling the results for women aged 40-49 in these six trials showed that the relative risk for breast cancer mortality was 0.85 (95% confidence interval 0.73-0.99) among screened women after 13 years of observation. These results are similar to prior meta-analyses based on older data. On average, the time until mortality benefits began to be observed was longer in women under 50 years than in older women. The analysis suggests that at least some of the mortality reduction was due to early detection of tumors before age 50.

ACS cites updates in the evidence from a number of individual RCTs of breast cancer screening and meta-analyses of these data, including the current (2002) USPSTF meta-analysis to justify their recommendation for annual screening in women beginning at age 40 years. In addition, ACS presents evidence from service screening (i.e., screening in the community setting), which appears to show mortality reductions similar to those seen in randomized controlled trials.

CTFPHC's current (2001) recommendation for screening mammography in the 40 to 49 age group was modified from the 1999 version that recommended exclusion of women in this age group from screening mammography during the periodic health examination. The updated version neither recommends the inclusion of the

maneuver in, or its exclusion from, the periodic health examination. This recommendation change is based on conflicting evidence regarding the benefits of screening women in this age group. CTFPHC cites the Canadian National Breast Screening Study, which did not show a reduction in mortality among women aged 40 to 49, and the two Swedish trials, which showed a statistically significant benefit of screening mammography in subgroup analyses. CTFPHC states that the most recent meta-analyses of 7 randomized controlled trials showed conflicting results. In one analysis, which included all 7 trials, a statistically significant relative risk reduction of 18% was shown, but a second analysis of only 2 trials found no effect.

RNZCGP also does not recommend routine screening for this age group because of the methodological problems in published studies. RNZCGP, however, does cite various meta-analyses showing mortality reductions ranging from 18-29% to 10% with screening mammography in women aged 40-49.

### Clinical Breast Examination (CBE)

There are some differences in the recommendations offered by RNZCGP, BWH, USPSTF, and ACS concerning CBE as a breast cancer screening measure. The differences stem chiefly from the lack of firm evidence that CBE alone reduces breast cancer mortality and from the perceived value of CBE in detecting palpable tumors.

Neither RNZCGP nor USPSTF recommends the use of CBE alone for breast cancer screening. RNZCGP recommends that CBE be used in conjunction with mammography, since mammography is more sensitive than CBE alone in screening asymptomatic women, but the sensitivity of both combined is greater than either alone. RNZCGP also states that tumors detected by CBE tend to be larger than those detected by mammography, which has a bearing on mortality. The additional effect of CBE on reducing breast cancer mortality beyond the benefit of mammography alone is therefore uncertain.

USPSTF states that there is insufficient evidence to recommend for or against routine CBE alone to screen for breast cancer. They cite evidence that reductions in breast cancer mortality in studies using mammography alone are comparable to those using mammography plus CBE. No studies have been done comparing CBE alone to no screening.

ACS and BWH, on the other hand, both recommend CBE in all women over age 20. ACS recommends that CBE be performed at least every three years for women in their 20's and 30's and annually beginning at age 40 whereas BWH recommends that it be done annually beginning at age 20. While BWH does not provide evidence for its recommendation, ACS presents a detailed discussion of available data. ACS concludes (based on weak and indirect evidence) that the contribution of CBE to breast cancer detection in asymptomatic women is small, especially in view of the high-quality mammography available today. They note however, that when done prior to mammography, CBE may identify an area of suspicion and/or help guide subsequent imaging exams. They further note that as the proportion of women receiving regular mammograms increases, the relative contribution of CBE to early breast cancer detection and its cost-effectiveness warrant renewed attention. ACS still recommends periodic CBE, however, in part

because the exam may provide the opportunity for clinicians to educate patients on breast cancer-related topics, including screening mammography. ACS also notes that its expert panel was divided in continuing to recommend periodic CBE, with some members believing that the evidence against the benefit of CBE was not strong enough to abandon the recommendation and others advocating elimination of the recommendation because it was not evidence-based.

## Breast Self-examination (BSE)

Although all of the groups have reservations about the value of BSE, they differ somewhat in their final recommendations to patients and health care providers.

There is general agreement on the lack of a clear benefit for breast self-examination (BSE) as a screening measure for breast cancer. CTFPHC maintains there is fair evidence of no benefit and good evidence of harm in teaching BSE to women aged 50 to 69 years and in women aged 40 to 49 years. CTFPHC was unable to make a recommendation for older women ( $\geq 70$  years) and younger women ( $< 40$  years) because of insufficient evidence. This current (2001) statement was a modification of a previous (1999) recommendation that there was insufficient evidence to make a recommendation for or against teaching of BSE. In making this revision, CTFPHC specifically cites evidence from randomized controlled trials that showed an increase in the number of physician visits for evaluation of benign breast biopsies in women who were taught BSE.

USPSTF concludes that there is insufficient evidence to recommend for or against teaching or performing BSE in any age group. USPSTF states that the accuracy of BSE is largely unknown, and that the available evidence shows a sensitivity of only 26-41% compared with clinical breast examination and mammography.

RNZCGP also does not recommend routine BSE because of a lack of evidence of clear benefit, although it does state that women should be advised to report any breast changes that they detect themselves to their physicians. In addition, RNZCGP advises women to "regularly look and feel for breast changes rather than follow a systematic method of examination."

While acknowledging that randomized controlled trials have found no mortality benefit from monthly BSE, BWH does not recommend either for or against its use as a screening method. BWH, however, also recognizes that many physicians will continue to recommend BSE because it is relatively inexpensive and noninvasive. The guideline's general conclusion is that patients can rely on annual CBE and screening mammography if they find BSE to be anxiety-provoking.

Among all the guideline groups, ACS makes the strongest recommendation in favor of BSE, even though they acknowledge the absence of definitive randomized clinical trial data from which to draw conclusions. Their recommendation is derived from expert opinion, which in turn is based on population-based studies showing that many breast cancers are self-detected. Earlier detection of palpable masses, they reason, can lead to earlier treatment in average-risk women under age 40. ACS also emphasizes that BSE heightens awareness of women to normal breast tissue, which makes it more likely for them to detect changes from normal. Thus, ACS advocates BSE instruction for women beginning in their 20's, with the dual provisos that women be told of both its benefits and limitations, and that it is

acceptable for women not to perform BSE. Women should be advised to report any new breast symptoms promptly to their health care provider. Finally, as with CBE, the ACS guideline panel was divided on whether to abandon the recommendation for BSE because of the lack of sufficient evidence.

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This Guideline Synthesis was prepared by ECRI on December 28, 1998. It was reviewed and verified by the guideline developers as of February 19, 1999. This Synthesis was modified by ECRI on April 12, 2001 to include guidelines from Scottish Intercollegiate Guidelines Network (SIGN) and CTFPHC. It was reviewed by these guideline developers as of May 24, 2001. This Synthesis was updated on September 19, 2001 to include a CTFPHC update. It was reviewed by CTFPHC as of October 8, 2001. This Synthesis was then updated on June 11, 2002 to incorporate new and updated Kaiser Permanente-Southern California (KPSC), RNZCGP and USPSTF guidelines. Recommendations from American College of Preventive Medicine (ACPM), Office of Medical Applications of Research (OMAR), and CTFPHC were also removed from this Synthesis following their withdrawal from the NGC Web site. This synthesis was updated again in 2002 to incorporate revised guidelines issued by USPSTF. In 2003, the 1997 ACS guideline was removed from this synthesis following the guideline's withdrawal from the NGC Web site. Content from the American College of Radiology (ACR), SIGN, and KPSC guideline summaries was removed from this synthesis on March 17, 2004 following the guidelines' withdrawal from the NGC Web site. The most current version of this Synthesis incorporates Brigham and Women's Hospital (BWH) recommendations and the 2003 updated recommendations from ACS.

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